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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,727	08/24/2001	Reiner L. Gentz	PF454P2	3532

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EXAMINER	
O HARA, EILEEN B	
ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,727	GENTZ ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,26,31,36 and 49-123* is/are pending in the application.

4a) Of the above claim(s) *1, 15, 26, 31, 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,15,26,31,36 and 49-123* ~~are~~ were subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1, 15, 26, 31, 36, and 49-123 are pending in the instant application. Claims 2-14, 16-25, 27-30, 32-35 and 37-48 have been canceled and claims 49-123 have been added as requested by Applicant in Paper Number 7, filed December 16, 2002, 2003.

Election/Restriction

2. Applicant's election with traverse of the subject matter of new claims 49-123, drawn to antibodies to TNFR-6 proteins and forming new Group VI, in Paper No. 7 is acknowledged. The traversal on pages 14-15 of the response is on the ground(s) that even assuming the Examiner were correct that the claimed methods are patentably distinct inventions, where two patentably distinct inventions appear in a single application, restriction remains improper unless it can be shown that the search and examination of both groups would entail a "serious burden", MPEP § 803. Applicants further assert that with respect to Groups I-IV, the Examiner has not indicated that the different Groups have a different status in the art, or a different field of search, beyond the statement that the different diseases and disorders named in the claims have different etiologies and therefore have different considerations for enablement. This is found persuasive, and Groups I-IV are rejoined. Applicants further assert that it would not be a serious burden to search the claimed methods of treatment (Groups I-IV) with the claimed nucleic acid molecules and antibodies (Groups V and VI, respectively), and that the search for TNFR-6 polypeptides used in the methods of treatment would clearly provide useful information for the polynucleotide and antibody claims, and for example, in many publications, both the polypeptide sequence and the nucleotide sequence encoding the said polypeptide commonly overlap, and a search for

polypeptides of the invention would encompass publications in which antibodies specific for the polypeptides of the invention are also disclosed, and thus a search and examination for the claimed methods, polynucleotides and antibodies would not entail a serious burden.

This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met for Groups I-IV (now rejoined) and Groups V and VI in the above restriction. The elected group drawn to antibodies, are classified in class 530, subclass 388.1, for example, which is a different class and subclass from that of the other groups. Also, a search for antibodies to a protein would constitute a different search than that of a search for the protein. It is old and well known in the art that antibodies have been generated without having purified protein, and antibodies to one protein may also cross-react with a related protein. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. As stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02.".

Also argued is that a search for one group would be overlapping and provide useful information about the other groups. However, the fact that some useful information may be obtained in the searches of one group for that of another group, and the fact that there may possibly be overlaps in the searches is not a sufficient basis for holding the restriction to be improper, because the search and examination of one group may not yield all of the necessary

information for the other group. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 15, 26, 31, 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 49-123 are currently under examination.

Specification

3.1 The abstract of the disclosure is objected to because it does not recite the invention to which the claims are directed, antibodies. Correction is required. See MPEP § 608.01(b).

3.2 Figures 2 and 3 of the instant application are presented on separate panels, and have been labeled correctly (for example, FIG. 2A-B) in accordance with 37 C.F.R. § 1.84(U)(1). However, the legends to Figures 2 and 3 on page 9 of the specification does not refer to Fig. 2A-B or Fig. 3A-P, respectively. Applicant is required to file an amendment under 37 C.F.R. § 1.312 to change the Brief Description of the Drawings and the rest of the specification accordingly. If, for example, Figure 2 is divided into Figures 1A and 1B then the Brief Description and all references to this figure in the specification must refer to Figures 1A and 1B.

3.3 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Antibodies to tumor necrosis factor receptors 6alpha and 6beta.

3.4 The use of the trademark "FLAG" has been noted in this application. It should be capitalized wherever it appears (for example, page 213 lines 24, 25 and 29) and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

3.5 On page 10 of the specification, the legend to Figures 7A-B, the last sentence states that TNFR6 alpha-Fc appears to block Fas ligand mediated apoptosis of Jurkat cells in a dose dependent manner as effectively as Fas **ligand**. However, from the experiment discussed in Example 9 on pages 213-214 and from examination of Figure 7A, it is demonstrated that TNFR6 alpha-Fc can block block Fas ligand mediated apoptosis of Jurkat cells as effectively as **Fas-Fc.** Fas ligand should be replaced with Fas-Fc at the end of section [0033] on page 10.

3.6 On page 22 of the specification, section [0075], TNFR-6□ should be replaced with TNFR-6 alpha.

Information Disclosure Statement

4. The sequences disclosed in the IDS filed Dec. 16, 2002 (Paper No. 8) have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

Advisory Information

5. The claims are interpreted such that the fragment of the antibody must also bind the protein. If Applicants intend otherwise, it is suggested the claims be amended to clarify this.

Claim Objections

6. Claims 53 and 115 are objected to because of the following informalities:

6.1 Claim 53 is objected to because there is no period after the number 53.

6.2 Claim 115 is objected to because "f" on the fourth line should be "of".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 82-114 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims require the specifically disclosed cDNA encoding the protein. Applicants' referral to the deposit of the cDNA clone deposited as ATCC Deposit Number 97810 on page 10 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an

affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 49-123 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8.1 Claims 50, 51, 71, 72, 83, 84, 104, 105 and 116 are indefinite because they encompass an antibody that binds to a polypeptide of SEQ ID NO: 2, and the claims from which they depend encompass an antibody that "specifically binds". The specification does not define the term "specifically binds" and it is not clear what this means, and it is not clear what the difference in scope between "binds" and "specifically binds" is.

8.2 Claims 49-123 are indefinite because claims 49, 57, 58, 63, 70, 77, 78, 82, 90, 91, 96, 103, 110, 111, 115, 119 and 120 encompass an antibody or fragment thereof that "specifically" binds to a polypeptide. The specification does not define the term "specifically binds" and since it is a relative term, it is not clear what this means. The other claims are rejected as being dependent claims. The rejection would be withdrawn if the word "specifically" were deleted.

Conclusion

9.1 No claim is allowed.

9.2 The art considered pertinent to the present application is Emery et al., PN 5,885,800, March 23, 1999 (cited by Applicants), which discloses a polypeptide identified as human tumor necrosis factor related receptor TR4 (see Fig. 1, SEQ ID NO: 2), which is 100% identical to the polypeptide of SEQ ID NO: 2 of the present application. This is not considered prior art, since the filing date of Emery et al. is Feb. 4, 1997 and the effective filing date of the instant application is Jan. 14, 1997 (provisional 60/035,496).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner